TULAREMIA

General points on treatment

Tularemia is an infection due to *Francisella tularensiss*. Natural infections occur following inhalation of the organism by occupationally exposed persons. As few as 10 – 50 orgar produce infection via the respiratory route but there has been no documented person-person transmission. After an incubation period that ranges from 1- 5 days for primary pneum (otherwise 1 – 14 days), the inhalation form of tularemia is manifested by fever, prostration, weight loss and respiratory symptoms.

Aminoglycosides are the drugs of choice and virtually all strains of *F. tularensis* are susceptible to streptomycin and gentamicin. Tetracyclines and chloramphenicol have been used successfully but are associated with higher relapse rates (1,2). Ciprofloxacin have been successfully used in clinical setting (1, 2, 3, 4, 5) and the bacteria are sensitive *in vitro* but data in patients with tularemia are lacking (2,3,4). Many antibiotics including all beta-lactam drugs are ineffective for the treatment of *F. tularensis* infections. *In vitro* data indicate susceptibility to rifampicin, sulphonamides and macrolides but there is a lack of clinical data to support a recommendation for clinical use (6, 7, 8).

Because of the mortality that could be anticipated with serious cases of inhalational tularemia, combined use of two antimicrobial agents of different classes, i.e. Gentamicin and Ciprofloxacin predicted to be effective should be considered; however, controlled studies to support a multiple drug approach are not available.

In case of tularemia meningitis, the preferred treatment option is chloramphenicol, 25 mg/kg iv, four times daily in both adults and children with similar oral doses as follow up therapy. (Treatment duration should be 21 days in view of the risk of relapse).

This guidance covers treatment regimens of suspected or confirmed clinical cases of tularemia whatever the clinical presentation and post exposure prophylaxis in case of suspected or confirmed exposure to *F. tularensis***.**

Recommendations are compiled from references 1-9.

RECOMMENDATIONS

In a mass casualty setting parenteral treatment may not be an option and recommendations for oral treatment should be followed. Otherwise oral therapy should be substituted when the patient's condition improves. In addition, the high bioavailability of some products (eg ciprofloxacin and doxycycline) makes initial oral therapy an option.

Name of active substance ➢ **Role in therapy and prophylaxis**	**Section**	**Treatment of suspected or confirmed clinical cases of Tularemia** Duration of treatment: 10 –21 days (as further indicated below under posology)	**Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen** Duration of prophylaxis: 14 days
Gentamicin ➢ **First line treatment**	**Posology** **Duration: 10 days**	**<u>Adults</u>** Standard doses for severe sepsis, such as 5 mg/kg iv once daily or 2.5 mg/kg twice daily	**<u>Adults</u>** NA
		<u>Children</u> 2.5 mg/kg iv three times daily	**<u>Children</u>** NA
	Contra indications	Should be considered in view of the prescribing information given in the different Member States.	
	Pregnancy and lactation	Given the seriousness of the condition the same product as in non-pregnant adults should be considered. It is recommended, when possible, to cease breastfeeding.	

Streptomycin ➢ **First line treatment**	**Posology** **Duration: 10 days**	**<u>Adults</u>** 1 g im twice daily	**<u>Adults</u>** NA
		<u>Children</u> 15 mg/kg im twice daily (maximum dose, 2 g)	 NA
	Contra indications	Should be considered in view of the prescribing information given in the different Member States.	
	Pregnancy and lactation	Given the seriousness of the condition the same product as in non-pregnant adults should be considered. It is recommended, when possible, to cease breastfeeding.	
Ciprofloxacin ➢ **Second line treatment** ➢ **First line prophylaxis**	**Posology** **Duration: 14 days**	**<u>Adults</u>** 400 mg iv twice daily followed by 500 mg orally twice daily	**<u>Adults</u>** 500 mg orally twice daily
		<u>Children</u> 10-15 mg/kg/day iv twice daily followed by 10 -15 mg/kg orally twice daily. The daily dose in children should not exceed that in adults.	**<u>Children</u>** 10 –15 mg/k orally twice daily
	Contra indications	Should be considered in view of the prescribing information given in the different Member States.	
	Pregnancy and lactation	Given the seriousness of the condition the same product as in non-pregnant adults should be considered. It is recommended, when possible, to cease breastfeeding.	

Ofloxacin ➢ **Alternative to ciprofloxacin**	**Posology**	**<u>Adults</u>** 400 mg iv twice daily followed by 400 mg orally twice daily	**<u>Adults</u>** 400 mg orally twice daily
	Contra indications	Should be considered in view of the prescribing information given in the different Member States.	
	Pregnancy and lactation	Given the seriousness of the condition the same product as in non-pregnant adults should be considered. It is recommended, when possible, to cease breastfeeding.	
Levofloxacin ➢ **Alternative to ciprofloxacin**	**Posology**	**<u>Adults</u>** 500 mg iv once daily followed by 500 mg orally once daily	**<u>Adults</u>** 500 mg orally once daily
	Contra indications	Should be considered in view of the prescribing information given in the different Member States.	
	Pregnancy and lactation	Given the seriousness of the condition the same product as in non-pregnant adults should be considered. It is recommended, when possible, to cease breastfeeding.	

<table>
<tr><td rowspan="4">Doxycycline

➢ Third line treatment

➢ Second line prophylaxis</td><td rowspan="2">Posology

Duration:
21 days</td><td><u>Adults</u>

100 mg iv twice daily followed by 100 mg orally twice daily</td><td><u>Adults</u>

100 mg orally twice daily</td></tr>
<tr><td><u>Children</u>

> 8 years and >45 kg: adult dose
> 8 years and <45 kg: 2.2 mg/kg iv twice daily
< 8 years 2.2. mg/kg iv twice daily (maximum 200mg per day)
followed by
same regimen orally</td><td><u>Children</u>

> 8 years and >45 kg: adult dose
> 8 years and <45 kg: 2.2 mg/kg orally twice daily
< 8 years 2.2. mg/kg orally twice daily
(maximum 200 mg per day)</td></tr>
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References

1. JAMA Consensus statement. Tularemia as a biological weapon. Vol. 285 No.21, June 6, 2001

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